Biochemical and Molecular Epidemiology of Cancer 177–190 (1986)

Toward the Decline of Lung Cancer

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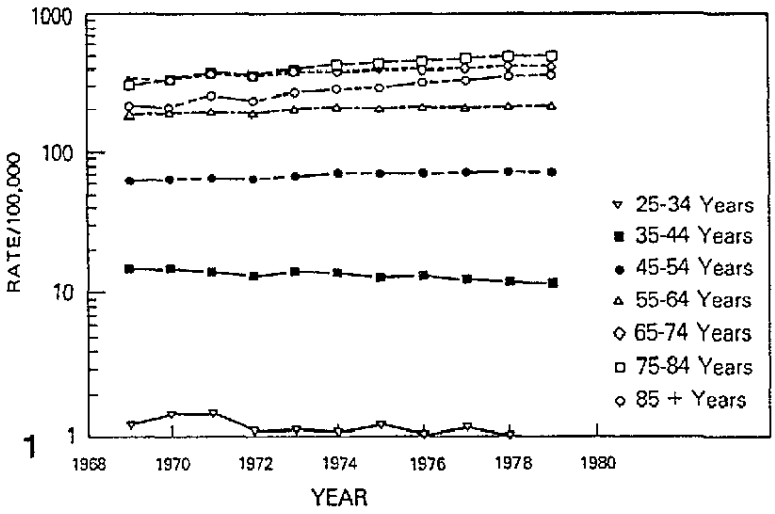
Recent declines in the rate of lung cancer among young adults in the United States and Europe cannot be explained completely by reductions in the prevalence of current smoking. The effect of other factors on trends in lung cancer incidence and mortality are discussed, including the role of smoking cessation, alterations in the tar and nicotine content of cigarettes, occupational exposure, air pollution, and nutrition.

Key words: lung cancer decline, smoking cessation, low-tar yield cigarettes, occupational exposures, air pollution, nutrition

During the past four decades there has been a dramatic increase in the incidence of lung cancer in men throughout much of the world. Lung cancer is the leading cause of cancer death in men in most countries, and in 1985 it will be the leading cause of cancer mortality in women in the United States [1]. An examination of sex-specific incidence rates in this country demonstrates a steady increase in the number of new cases of disease, especially among the older cohorts. The rate of increase is declining among younger men, while among women the incidence rates are still climbing rather sharply.

Data from the National Center for Health Statistics show a drop in age-specific mortality among men born after 1930 and possibly among women born after 1940 [2] (see Figs. 1, 2). Among white males, decreases in the incidence rates for cohorts aged 25–34 years were found in both the Third National Cancer Survey [3] and in the more recent Surveillance, Epidemiology End Results (SEER) data [4]. Increases in lung cancer incidence for white men aged 35–44 did not peak until about 1970, when the Third National Cancer Institute data were collected, declining somewhat by the end of the 1970s. Mortality rates among this group decreased from 15 to 12 per 100,000 per year between 1969 and 1979 [5]. While mortality rates among white males between 35 and 44 years of age were stable during the 1970s, increases were still being recorded among the older age cohorts. Incidence and mortality data indicate that rates may also be declining among women under 35 years of age, although sample sizes are too small to be certain [5].

Received May 28, 1985.



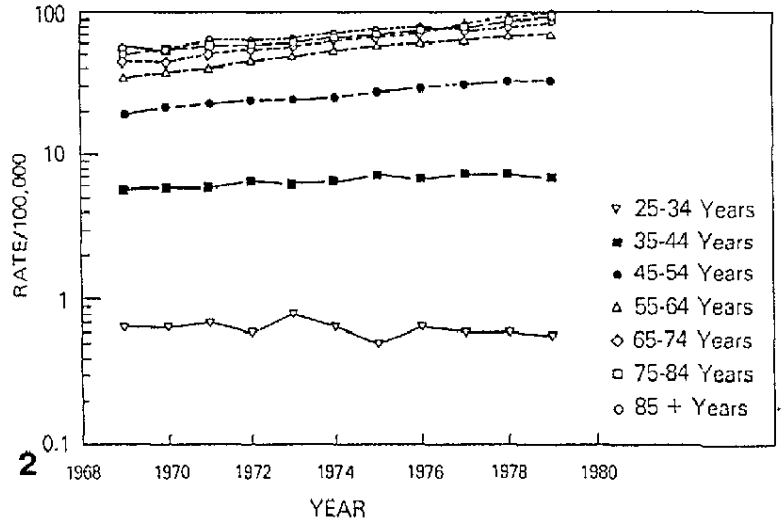


Fig. 1. Age-specific US lung cancer mortality trends among white males. Reprinted from Devesa et al, with permission [5].

Fig. 2. Age-specific US lung cancer mortality trends among white females. Reprinted from Devesa et al, with permission [5].

The purpose of this communication is to review possible reasons for secular trends in the incidence and mortality for lung cancer. The extent to which changing patterns of tobacco consumption in the United States and the rest of the world have contributed to these trends will be considered in addition to the role of smoking cessation, alterations in the tar and nicotine content of cigarettes, occupational factors, air pollution, and diet. It is hoped that this epidemiological exercise will add to the understanding of factors that may affect the downward trend of lung cancer incidence in younger, United States' male cohorts.

RESULTS

Tobacco Consumption

Smoking habits, especially in the United States, have undergone significant change during the past few decades. In 1955, over one half (54%) of the adult (≥20 years) male population and 27% of adult females were present smokers of cigarettes [6]. Adult cigarette smoking decreased among men by 1965 to 49% and increased among women to 32%. By 1980, it was estimated that these percentages had declined to 38% of adult men and 30% of adult women. Among men, this decline was greatest among the youngest and oldest age groups, with a 33% decline among 20–24 year-olds and a 37% decline among men over the age of 65 (Table I).

The decrease in the proportion of cigarette smokers between 1965 and 1980 was not as great among women. There were 22% fewer smokers among women aged 20–24 and an increase of 75% among women over the age of 65, from 10% in 1965 to 17% in 1980.

Consistent with these changes in smoking patterns, the proportion of never-smokers by age cohort has also changed [2] (Fig. 3). The percentage of never-smokers in the population increased for all men less than 45 years of age and for women less than 35 years old. Almost one-half of the men below the age of 25 had never smoked cigarettes in 1980 compared to less than one-third in this age group in 1965. Among women below 25 years of age, 50.8% claimed to be never-smokers in 1965 versus 56.3% in 1980. Thus, by 1980, young adult men and women were smoking to about the same extent.

What effect will this change in smoking habits have on lung cancer rates? It has been established that trends in mortality rates from lung cancer closely parallel changes in per capita cigarette consumption after a sufficient lag period has elapsed. Thus, the increased smoking prevalence in men born between 1910 and 1930 and in women born between 1920 and 1950 in the United States no doubt led to the "epidemic" of lung cancer occurring in the 1970s and 1980s [2]. This displays the strong coherence of the association of smoking behavior by birth cohort and subsequent mortality experience. In England and Wales, where per capita cigarette smoking plateaued earlier than it did in the United States, there has been a steady decline in the number of deaths from lung cancer, especially among younger male cohorts,

TABLE I. Percentage Change in the Proportion of Present and Former Smokers Among Adults in the United States by Sex, 1965 vs 1980

Age group (years)	Percent change in proportion			
	Present smoker[a]		Former smokers[b]	
	Male	Female	Male	Female
20–24	−33	−22	+34	+51
25–34	−29	−28	+40	+45
35–44	−27	−40	+34	+97
45–64	−21	−4	+53	+99
≥65	−37	+75	+69	+215
All ages ≥65	−27	−13	+50	−91

[a]Present smoker has smoked at least 100 cigarettes and non smokers include occasional smokers.
[b]Former smokers stopped smoking at least 1 year prior to interview.
From the Surgeon General, 1982 [2].

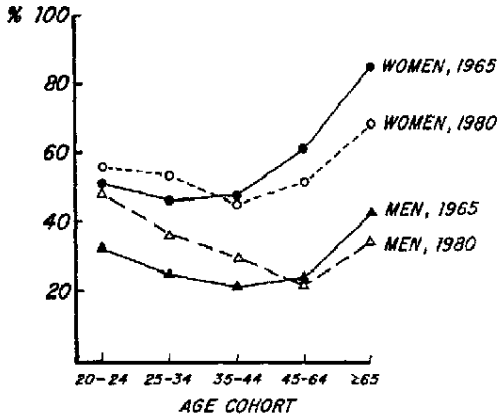


Fig. 3. Percentage distribution of those who have never smoked cigarettes in the United States by age and sex, 1965 vs 1980. From the Surgeon General, 1982 [2].

presumably as the relative proportion of smokers in the younger generations diminishes.

To illustrate this point, a comparison of mortality data from different time periods is informative [7] (Table II). In investigating the trend of decreasing mortality from lung cancer among the younger cohorts of men, the 50% decline in death rates cannot be adequately explained by the 20% decline in smoking prevalence [8]. Similarly, an analysis of prospective data of 10,000 males has shown that only 55% of the difference in lung cancer incidence between geographic areas in Finland and Norway between 1953 and 1962 could be predicted by variations in smoking habits [9]. A second analysis of these data, using risk indices for 1975–1979, displayed a slightly better fit (64%) when plotted against the original smoking indices for 1962, but still left over one third of the variation unexplained [10].

Smoking Cessation

There is no doubt that the cessation of tobacco smoking stops the increase in excess risk associated with continued use of tobacco products [11–15]. In a case-control study conducted by our group [16], we found that among subjects who had smoked for 20 years or more, cessation of cigarette smoking did not alter the risk of lung cancer for about 3 years, followed by a gradual decline in risk approaching that for a nonsmoker after 10 to 15 years. The speed of the decline was dependent on the history of the amount and duration of smoking. The lag period for the reduction in risk associated with smoking cessation is affected in part by selection bias. For instance, smokers with symptomatic conditions will often quit smoking because of discomfort or their physician's advice. This effect diminishes with time, because of selective mortality, since people in poor health will die more rapidly than people in good health.

US trends in smoking cessation correspond inversely to secular patterns in the proportion of current smokers. Between 1965 and 1980, the proportion of ex-smokers among adults in the United States increased from 20 to 30% among men and 8 to 16% among women (see Table I). Increases in the relative proportion of ex-smokers in the population were greater with increasing age for both sexes. Also, the increased

TABLE II. Decreases in Lung Cancer, Comparing 1978 Data With Data for the Worst-Affected Generations of Men in England and Wales and in the United States

	England and Wales				*United States*			
	Worst-affected generation (born ca 1910–1911)[a]		Rates for 1978 compared with those for worst-affected generation		Worst-affected generation (born ca 1910–1911)[a]		Rates for 1978 compared with those for worst-affected generation	
Age (years)	Mortality/ million men	Period of observation	Mortality/ million men in 1978	Decrease (%/year)[b]	Mortality/ million men	Period of observation	Mortality/ million men in 1978	Decrease (%/year)[b]
30–34	40	1941–45	17	58/35	24	1958–62	17	30/18
35–39	98	1946–50	63	36/30	73	1963–67	62	15/13
40–44	253	1951–55	138	45/25	219	1968–72	192	12/8
45–49	597	1956–60	385	36/20	502	1973–77	480	4/3
50–54	1,234[c]	1961–65	1,047	15/15	?	1980	1,021	—[e]
55–59	2,219[d]	1966–70	1,912	14/10	?	1985	1,647	—[f]
60–64	3,577[d]	1971–75	3,315	7/5	?	1990	2,625	—[g]
65–69	5,018	1978	5,018	—	?	1995	3,557	—[g]

[a]These are the generations with the highest death rates at ages 35–44, when substantial effects of smoking first became evident. However, if in the future the number of cigarettes smoked per individual will decrease, or the effective dose of noxious chemicals per cigarette will decrease, the benefits at some particular attained age to these two worst-affected generations may be greater than to the immediately previous generations. The maximum American lung cancer rates in old age may therefore be seen, at around the turn of the century, in the generation born in the few years before this "worst-affected" generation.

[b]Percentage decrease, comparing age-specific mortality in 1978 with that for the worst-affected generation (born 1910–11 in England and Wales, born 1927–28 in the United States).

[c]Might have been materially larger but for changes in cigarette composition.

[d]Would have been materially larger but for changes in cigarette composition.

[e]US mortality at ages 50–54 years should reach a maximum by ca 1980.

[f]US mortality at ages 55–59 years is still rising.

[g]US mortality at ages 60–64 and 65–69 years is still rising rapidly.

Reprinted from Doll and Peto [7], with permission.

percentage of former smokers during the 15-year period was larger among women than among men within each age category. This may be accounted for, in part, by the much larger percentages of ever-smokers and former smokers among men. For instance, 28% of men over the age of 64 were categorized as former smokers in 1965 compared to 4% of women. These percentages increased to 47% of men in 1980 (representing a 69% increase) and 14% of women (representing a 215% increase).

To what extent has smoking cessation contributed to the apparent reversal in the spiralling rate of lung cancer deaths? It was noted earlier that cigarette smoking cessation would not immediately produce a reduction in risk of lung cancer for smokers, but would certainly prevent large increases in risk similar to those experienced by continuing smokers. While it is difficult to assess fully the effects of tobacco smoking cessation on recent trends in lung cancer mortality, several prospective studies present evidence that smokers who quit do indeed reduce their risk of lung cancer. Data from 20 years of observation on male British doctors showed that mortality decreased with the duration of cigarette smoke cessation, although at the end of 15 years it was still two times that of never-smokers [12]. Two other prospective studies, the Multiple Risk Factor Intervention Trial (MRFIT) [17] in the United States and the Whitehall Study of London Civil Servants in England [18] have examined the relationship of smoking cessation to lung cancer risk. The MRFIT Study, including 12,866 high risk (heavy cigarette consumption, high blood pressure, high serum cholesterol) men, showed 81 deaths from lung cancer in the intervention group compared to 69 deaths among the usual care group after 7 years of follow-up. The difference between these mortality rates was not significant. Smoking intervention, including basic behavioral modification techniques and hypnosis, reduced the proportion of ever cigarette smokers in the study group from 63.8 to 32.3% after 72 months. The proportion of ever-smokers among the usual care group was reduced from 63.5% to 45.6% after 72 months. This study might be used to support the contention that smoking cessation does nothing to reduce the risk of lung cancer. One needs to ask, however, whether a reduction in mortality should have been expected. Participants in the MRFIT program were selected specifically because they were considered at high risk of coronary heart disease. They were generally all heavy smokers at the outset of the trial. American Cancer Society data on smoking cessation show that long-term smokers (20 or more years) of a pack or more of cigarettes per day had much less substantive risk reduction than did people smoking less than a pack per day before quitting [19,20] (Table III). When mortality ratios for ex-cigarette smokers compared to never-smokers were analyzed by years of smoking cessation, quitters for 10 years or more had mortality ratios of 1.08 among light smokers in contrast to 1.50 among heavy smokers. Thus, substantial reductions in mortality were not as apparent in previously heavy smokers. The MRFIT participants were not only

TABLE III. Mortality Ratio of Current Cigarette Smokers and Ex-smokers*

No. of cigarettes smoked per day	Current cigarette smokers	Stopped (years)		
		1	1–10	10+
<20	1.61	2.04	1.30	1.08
20+	2.02	2.69	1.82	1.50

*The mortality ratio of men who never smoked was set at 1.00.
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heavy, long-term smokers, but the follow-up data reported were only for a 7-year period—perhaps too short to demonstrate a significant change.

A report of 10 years of observation in the Whitehall study, a randomized trial of smoking cessation in 1,445 male smokers aged 40–59 years who were at high risk of cardiorespiratory disease, showed a small, significant difference in mortality between the intervention group (I) and normal care group (NC) [18]. The I group, consisting of 714 smoking men, were given advice on smoking cessation, while the NC group of 731 men were left alone. Lung cancer death rates were reduced to a similar extent in participants of both groups who gave up smoking. Overall, lung cancer mortality was 23% lower in the I group (calculated as the estimated proportionate reduction in 10 year risk), although this reduction was not significant. Two reasons for the absence of an effect may have been that 1) the one third of smokers who gave up cigarettes in the I group continued to smoke pipes and cigars, and 2) while a decline in lung cancer risk among heavy smokers may be expected by the end of 9 years, differences in the number of cigarettes smoked per day in the I and NC groups were small, averaging three or four cigarettes by the final postal inquiry.

Tar and Nicotine Yields

The dose-response relationship found between the risk of lung cancer and the number of cigarettes smoked per day prompted the belief that lower tar in cigarettes would lead to a diminution in the risk of lung cancer. Reports in the literature have been ambiguous regarding the effects on mortality of these reductions in tar yield [21–33], although there now appears to be a clearer picture of possible benefits [23]. Peto and Doll [34] have proposed that much of the decreasing rate of lung cancer in British men before the age of 50 years may have resulted from the introduction of the filter-tipped cigarette. The British data show that the younger cohorts smoke 20% fewer cigarettes than the older cohorts—a difference that does not alone account for reductions in the rate of lung cancer found among men under the age of 45 years (see Table II). This finding conforms with expectations, since individuals who are less than 50 years will have been smoking cigarettes on average since the middle 1950s when substantial tar reductions in cigarettes were taking place. Changes in mortality rates that have occurred in cohorts older than 50 years are difficult to assess, since the majority of these patients began smoking with nonfilter cigarettes. Thus, studies of trends in mortality for this age group will include a large number of people who smoked low-tar cigarettes for only a fraction of their smoking lives (Goodman and Wynder, unpublished data, 1985) (Figs. 4, 5). Other problems such as smoking compensation, changes in cigarettes smoked per day, and tobacco smoke inhalation may also affect these findings. For instance, between 1965 and 1980, the percentage of male adult ($\geqslant$20 years) smokers who smoked at least 25 cigarettes per day rose from 25 to 34%, while the proportion of individuals smoking less than 15 cigarettes per day fell from 28 to 23% [6] (Fig. 6). Among women, these percentages were even more divergent, rising from 14 to 24% of individuals smoking more than 24 cigarettes per day and falling from 44 to 34% of women smoking less than 15 cigarettes per day.

The tar yield of both filter-tipped and nonfilter cigarettes in the United States and in most other industrialized societies has declined sharply over the past few decades (Fig. 7). Smokers who do not compensate in full for the reduction in nicotine by smoking more cigarettes, puffing more frequently or with greater volume, or by

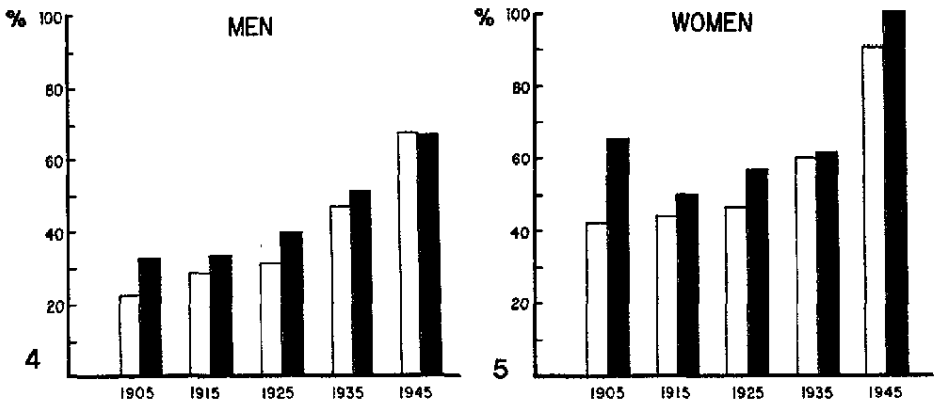


Fig. 4. Filter cigarette usage as a percentage of lifetime smoking experience by birth cohort. Open bars, cases (N = 969). Closed bars, controls (N = 1,938).

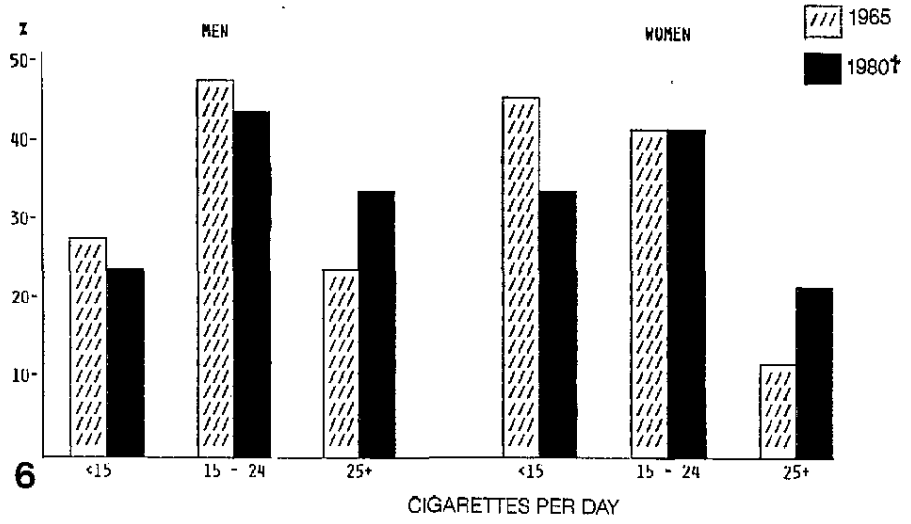
Fig. 5. Filter cigarette usage as a percentage of lifetime smoking experience by birth cohort. Open bars, cases (N = 375). Closed bars, controls (N = 749).

inhaling more deeply can expect to decrease their risk of lung cancer somewhat. Such a decrease would occur primarily among long-term smokers of low-yield cigarettes (ie, <10 mg tar). An assessment of the effect of these changes in smoking habits is difficult because, to date, relatively few smokers have smoked low-yield cigarettes for more than 10 years: about 2% of our male and 4% of our female controls. As suggested in a recent report [33] and in accordance with our data, it is probable that the risk of lung cancer may be measured in direct proportion to the tar yield of the preferred brand of cigarettes smoked, once appropriate adjustment has been made for duration and amount.

Occupational Factors and Air Pollution

Although there is a large attributable risk of smoking to lung cancer, there is no doubt that lung cancer is a multifactorial disease. A number of occupational exposures have been established as risk factors for lung cancer, including exposure to arsenic, asbestos, bischloromethyl ether, chromium, ionizing radiation, mustard gas, nickel, and polycyclic hydrocarbons in soot, tar, and oil [35]. Furthermore, these substances may not be representative of the full spectrum of potential carcinogens. Weak risk factors to which a large proportion of the population is exposed may produce substantial changes in the background of lung cancer deaths. Since many of the substances listed above have been in use for less than the average induction period for lung cancer, it is probable that current mortality reflects early stages in what may be an upward trend in rates. Doll and Peto [7] have criticized the Occupational Safety and Health Administration estimates [36] of the proportion of all cancers attributable to occupation (20% or more) on the basis of what they deem to be severe overestimation of the number of individuals in the United States who are heavily exposed to occupational carcinogens.

It is difficult to separate the effects of smoking and socioeconomic status from occupational and other factors [37] (Fig. 8). For instance, there is a strong interaction



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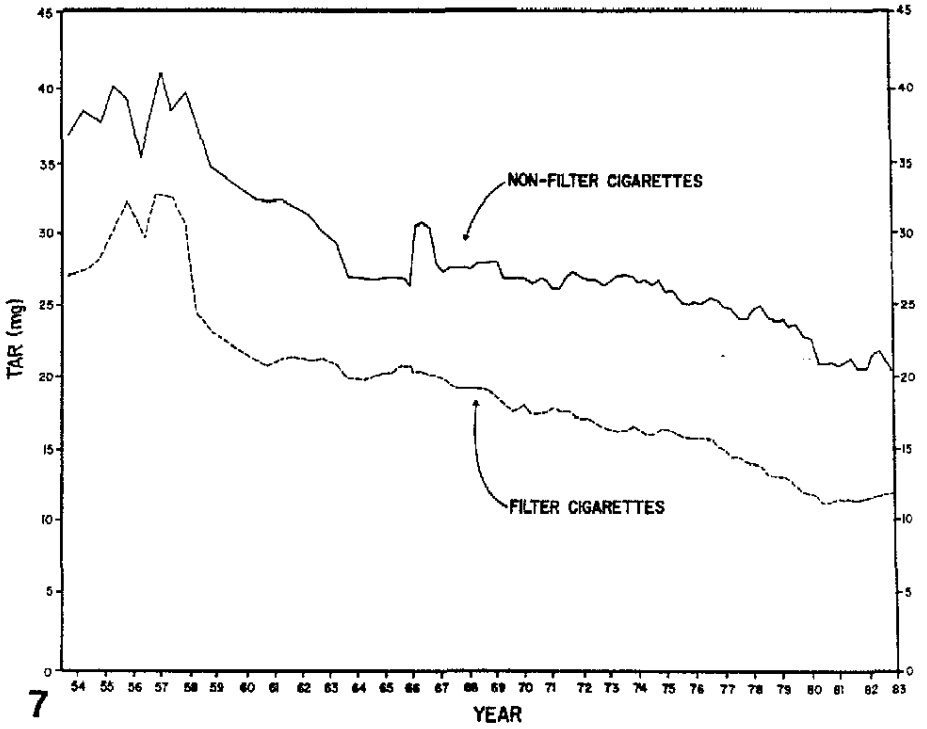

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Fig. 6. Percentage distribution of adult current smokers by grouped number of cigarettes smoked per day and sex, 1965 vs 1980. A current smoker has smoked at least 100 cigarettes and now smokes (includes occasional smokers). The 1980 data are for the last 6 months of 1980. From the Surgeon General, 1983 [6].

Fig. 7. Sales-weighted average tar deliveries, 1954–1983.

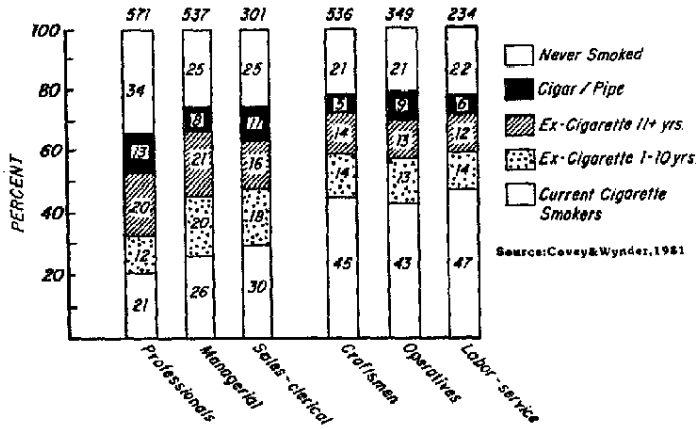

Fig. 8. Age-standardized smoking rates by occupational level of white male controls aged 41 through 70 years. Reprinted from Covey and Wynder [37], with permission.

between smoking and asbestos on the risk of lung cancer. The importance of testing for synergy between smoking (and socioeconomic status?) and these occupational exposures seems particularly important in view of the fact that there appears to have been no increase in the proportion of never-smokers developing lung cancer over the past 35 years [2,6]. Doll and Peto [7] attributed approximately 11,000 lung cancers to occupational factors in the United States, comprising 15% of male and 5% of female lung cancers. They recommend, and we concur, that there is a strong need for a case-control study based on a representative sample of US cases to clarify the relationship between smoking and occupation and the rate of lung cancer.

Air pollution has been investigated quite extensively in association with the risk of lung cancer because of the direct route of exposure and urban/rural differences in the rate of lung cancer unexplained by variations in tobacco consumption [38]. A large number of pollutants have been identified as carcinogens based on animal and occupational evidence [39,40], which has led to speculation of a causal relationship. The low rate of lung cancer in nonsmoking Seventh-Day Adventists living in Los Angeles or Greeks and Japanese living in heavily polluted Athens and Yokohama suggests that if there is an effect of air pollution on lung cancer risk it is small at best.

Nutrition

Another consideration is whether improvements in the dietary status of young adults may have added to the current trends in the decline of lung cancer incidence in the United States among this group. The role of dietary fat, fruits and vegetables, vitamin A, retinoids, and other micronutrients in the etiology of lung cancer has been the subject of a great number of recent investigations. Examinations of nutritional factors in the induction of lung cancer are difficult not only because of the overwhelming affect of tobacco smoke on risk but also as a result of the problems inherent in obtaining reliable dietary information. These problems have been reviewed by us in some detail in an earlier article [41]. As a result of these and other research obstacles, it is premature to come to any conclusions regarding the effect of nutritional excesses, deficiencies, or imbalances on the incidence of lung cancer. In spite of these reserva-

tions, two prospective studies with sample sizes large enough for appropriate statistical analysis provide suggestive evidence that daily consumption of green-yellow vegetables reduces the risk of lung cancer [42,43]. The relatively low incidence of lung cancer in Japan compared to that in the United States while caused, in large part, by differences in smoking patterns, may also be influenced by dietary differences [43]. Although the comparatively low consumption of fruits and green and yellow vegetables in Japan in the past would be inconsistent with the hypothesized protective effect of β-carotene, the intake of dietary fats, which may also enhance lung carcinogenesis, is also lower.

Doll and Peto [7] have posited that a reduction of US lung cancer deaths by 20% may be brought about by dietary means. We regard this issue as open. Investigations of macro- and micronutrients, especially of carotinoids on lung cancer risk are indicated. Case-control studies of lung cancer and nutrition must be conducted in a manner allowing for appropriate adjustment for smoking habits and socioeconomic status. Furthermore, we need to recognize that it may not be possible to obtain reliable dietary histories from cancer patients. Prospective studies with large-scale blood collection and storage for later analysis should be initiated to resolve the issue [44].

DISCUSSION

When the link between tobacco smoking and the risk of lung cancer was established in the early 1950s, it was apparent that the incidence of lung cancer would soon become the leading cause of cancer death among men and, perhaps in the future, among women. This prediction has unfortunately been realized.

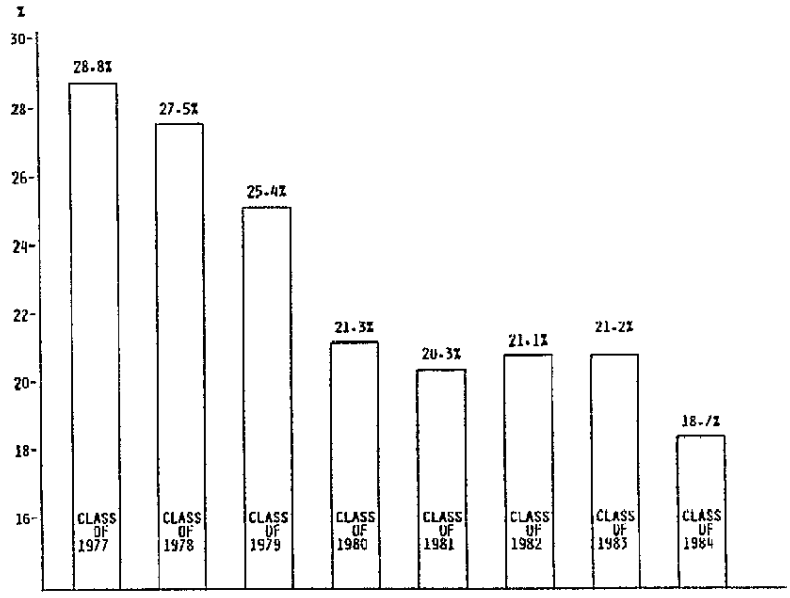

Fig. 9. Teenage smoking trends: daily smoking by high school graduates. Reprinted from the National Institute on Drug Abuse [47], with permission.

Following the release of the first Surgeon General's Report in 1964 [45] there have been gradual changes in smoking habits in the United States in addition to overall reductions in the tar yields of cigarettes. First, there was a sharp increase in males who quit smoking, especially among the middle-aged, upper-income groups. This was followed by a rise in the proportion of never-smokers among young men. These trends have led to an approximate 50% reduction in the percentage of male smokers compared to rates 30 years ago.

Women have also begun to stop smoking in increasing numbers, although not to the same extent as men. The overall percentage of female smokers, however, has doubled since 1950. Hence, the rate of new lung cancer cases continues to climb, and it is expected that the rate of this incline will not fall off for years to come.

Superimposed on these changes in the prevalence of cigarette smoking is the fact that the tar yield of American-manufactured cigarettes is about one half of what it was in 1950. Since most smokers are unlikely to compensate completely for this decline in tar yield, it is likely that smokers of low-tar yield cigarettes will reduce their risk of lung cancer significantly, an effect mostly to be seen among young cohorts. Efforts to reduce further the tar yields of cigarettes on the market should continue. The average tar yield of cigarettes should not exceed 10 mg.

Obviously, occupational carcinogens need to be controlled to the greatest extent possible. Air pollution, though unlikely to affect the risk of lung cancer, should be monitored and reduced for other public health reasons such as general hygiene. At this time, no specific dietary advice can be given for the possible prevention of lung cancer.

Those of us who have been involved in etiological research on tobacco-related cancers may derive some satisfaction from the turnaround in the lung cancer rates in most of the developed world. Anti-smoking campaigns have been obviously successful and should now focus on high risk groups such as women and lower income smokers. Young people should be admonished not to start smoking or, if they have already done so, to quit. That these preventive efforts have been fruitful is evidenced by a recent report released by the National Institute on Drug Abuse showing that the prevalence of teenage smoking continues to decline [46] (Fig. 9). The reduction in the risk of lung cancer in individuals who quit offers a special incentive to those in public health whose goal is the elimination of a preventive disease. We who have expended a great deal of energy toward the reduction of lung cancer and the tobacco-related diseases can now see light at the end of the tunnel.

ACKNOWLEDGMENTS

The authors thank Ms. Sheila Petty and Ms. Roz Fieland for their editorial assistance in the preparation of this manuscript. This study was supported by Public Health Service grant CA-17613 from the National Cancer Institute.

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